1: Mol Microbiol 1994 Sep;13(6):1093-100 Related Articles, Books, LinkOut

Anthrax toxin lethal factor contains a zinc metalloprotease consensus sequence which is required for lethal toxin activity.

Klimpel KR, Arora N, Leppla SH.

Laboratory of Microbial Ecology, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland 20892.

Comparison of the anthrax toxin lethal factor (LF) amino acid sequence with sequences in the Swiss protein database revealed short regions of similarity with the consensus zinc-binding site, HEXXH, that is characteristic of metalloproteases. Several protease inhibitors, including bestatin and captopril, prevented intoxication of macrophages by lethal toxin. LF was fully inactivated by site-directed mutagenesis that substituted Ala for either of the residues (H-686 and H-690) implicated in zinc binding. Similarly, LF was inactivated by substitution of Cys for E-687, which is thought to be an essential part of the catalytic site. In contrast, replacement of E-720 and E-721 with Ala had no effect on LF activity. LF bound 65Zn both in solution and on protein blots. The 65Zn binding was reduced for several of the LF mutants. These data suggest that anthrax toxin LF is a zinc metallopeptidase, the catalytic function of which is responsible for the lethal activity observed in cultured cells and in animals.

PMID: 7854123 [PubMed - indexed for MEDLINE]

Display Abstract Sort Save Text Clip Add Order